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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
03/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/692,537	KLUWE, LAN	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,8-10,14 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,8-10,14 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on January 16, 2008 has been entered.

Preliminary Remark

Claims 1, 4-7, 11-13, and 15-18 have been canceled.

Claims 2, 3, 8-10, 14, and 19 are pending and are under prosecution herein.

Claim Rejections - 35 USC § 112

The rejection of claim 8 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on April 17, 2007 is withdrawn in view of the Amendment received on January 16, 2008.

New Ground of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2, 3, 8-10, 14, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite for reciting the phrase, "or preferably four," because it is unclear whether the limitation is an actively required limitation or not.

Removing the term, "preferably" would overcome this rejection.

Claim 19 recites the phrase, "determining whether an offspring of an individual afflicted with a phakomatosis, wherein said phakomatosis is a tumor suppressor gene disease *has an increased risk of developing the tumor suppressor gene disease comprising…*" does not make grammatical sense.

Applicants are advised to amend the entire pending claims so that the term, "tumor suppressor gene disease" is replaced with the term, "phakomatosis," so as to maintain consistency in claim terminology and breadth.

Claims 2, 3, 8-10, and 14 are indefinite by way of their dependency on claim 19.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 8-10, 14, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining whether an offspring of an individual afflicted with neurofibomatosis has an increased risk of developing said neurofibromatosis, does not reasonably provide enablement for a method of determining whether an offspring of an individual afflicted with <u>any</u> type of phakomatosis. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

The Breadth of the Claims & Enablement Issues:

The term, "phakomatosis" is used to describe a group of congenital hereditary developmental anomalies involving tissues of ectodermal origin, examples of which includes neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, von Hippel-Lindau disease, etc.

The specification demonstrates their method drawn only to a single species of phakomatosis, that is neurofibromatosis, but fails to demonstrate that their method is also applicable to other conditions embraced by the broad terminology, "phakomatosis."

The enablement issue is raised because the disclosures of the instant specification, when viewed in conjunction with the unpredictability and state of the prior art, does not reasonably convey to a skilled artisan that the method as claimed can be practiced fully commensurate in scope of the claimed breadth.

Amount of Guidance:

The instant application's disclosure and guidance is directed solely to a single species of phakomatosis, neurofibromatosis.

The entire specification's guidance is directed to the use of polymorphous microsatellite markers which are located in genes which are implicated with neruofibromatosis, NF1 and NF2 (page 9), evaluation of said markers (page 10), and the discussion of results therefrom (page 10, bottom to page 11, and page 12).

There is simply no discussion or guidance in the specification which would guide a skilled artisan to practice the invention drawn to other species embraced by the term, "phakomatosis."

Nature of the Invention, Unpredictability in the art, & State of prior art

Nature of the invention relates to correlation of gene mutations which remains highly unpredictable in the art.

Lucentini et al. (The Scientist, 2004, vol. 18), titled his article, "Gene Association Studies Typically Wrong," and states, "[t]wo recent studies found that typically, when finding is first published linking a given gene with a complex disease, there is only roughly a one-third chance that studies will reliably confirm the finding (page 2 of the print out). This is consistent with the teachings of Wacholder et al. (Journal of National Cancer Institute, 2004, vol. 96, no. 6, pages 434-442) who notes that, "[t]oo many reports of association between genetic variants and common cancer sites and other ***complex diseases*** are false positives (see abstract). Ioannidis (Nature Genetics, 2001, vol. 29, pages 306-309) further supports this conclusion in pointing out that the heterogeneity of results among different studies of genetic polymorphisms (see abstract).

Finally, Tucker et al. (Journal of the National Cancer Institute, April 2000, vol. 92, no. 7, pages 530-533), in discussing phakomatosis, states, "Loss of heterozygosity (LOH) appears more common in plexiform neurofibromas than in dermal neurofirbromas. Most NF1 tumors appear to have loss of neurofirbromas but ***not necessarily LOH***, some may have ***subtle second mutations***." (page 530, 1st column bottom paragraph to page 530, 2nd column, 1st paragraph)

Level of the Skilled Artisan & Conclusion

While the skill level of the artisan in question may be high, based on the unpredictability of complex human disease, as evidenced by the those of skilled practitioners' statement discussed above, one of skill in the art would not be able to practice the invention fully commensurate in scope of the claims without undue experimentation.

Claim Rejections - 35 USC § 103

The rejection of claims 2, 3, 8, 9, 14, and 19 under 35 U.S.C. 103(a) as being unpatentable over Allione et al. (International Journal of Cancer, 1998, vol. 75, pages 181-186) in view of Cohen et al. (U.S. Patent No. 5,945,522, issued August 31, 1999) and Skolnick et al. (U.S. Patent No. 5,624,819, issued April 29, 1997), made in the Office Action mailed on April 17, 2007 is withdrawn in view of the Amendment received on January 16, 2008, amending the claims to become drawn to a method of determining whether an offspring of an individual is afflicted with phakomatosis.

Double Patenting - Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 2, 3, 8-10, 14, and 19 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,660,477 (herein, '477 patent), made in the Office Action mailed on April 17, 2007 is maintained for the reasons already of record.

Applicants state a terminal disclaimer will be filed upon indication of allowable subject matter in the application (page 9, bottom to page 10, Response).

As there is no terminal disclaimer filed as of the date of the instant office communication, the rejection is maintained for the reasons of record.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claims 1-16 of '477 patent are drawn to a method of determining whether an offspring of an individual afflicted with neurofibromatosis, wherein the method comprises the steps of amplifying polymorphic microsatellite markers from tumor and blood samples from the individual afflicted with neurofibromatosis, followed by the amplification of the same polymorphic markers from the offspring from the blood sample, followed by the comparison of the markers from that of the offspring to those of the individual.

Claims 1-16 of the '477 patent are a narrower species drawn to a particular type of condition, while the claims of the instant application is drawn to a genus of tumor suppressor gene disease. Hence, claims of the '477 patent are narrower species of the genus claims of the instant application.

In the instant situation, the narrower species claims necessarily renders the genus claims of the instant application obvious in an "anticipatory" way.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the

status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
3/16/2008